Amendments to the Specification

On page 2, please replace paragraph [0005] with the following:

[0005] One of the shortcomings of many of the prodrugs and derivatives of rapamycin is the complicated synthesis involved in preparing the prodrug or derivative, where additional synthetic steps are required to protect and deprotect certain positions. Also, care must be taken in designing prodrugs and derivatives to preserve activity of the compound and to not sterically hinder positions necessary for protein binding or other cellular interactions. Derivatives having a shorter overall chain length and/or overall steric bulk (volume) in the chemical moiety attached to the compound are less likely to produce steric ~~hinderance~~hindrance of binding sites. It would be desirable to design a derivative that has a shorter chain length or smaller size in the attached moiety.

On page 18, please replace paragraph [0073] with the following:

[0073] Fig. 3C shows the stent of Figs. 3A-3B in cross-sectional view. The view is taken through stent tubular member 24, with adjacent tubular members visible. The stent body, and more specifically each tubular member, is coated with drug or with a polymer-drug composition, for release of drug from the stent at a target site. As will be more fully described below, the drug or drug-polymer layer is applied to the external surface of the stent, and can be deposited to achieve a uniform deposition ~~thickess~~thickness or a non-uniform deposition thickness. Fig. 3C illustrates the embodiment where the drug-polymer layer 32 is applied non-uniformly so that the external stent ~~sufacesurface~~ has a thicker drug or drug-polymer coating than the internal stent surface.

On page 18, please replace paragraph [0075] with the following:

[0075] The drug is coated directly onto the stent by, for example, applying a solution of drug to the stent surface by dip coating, spray coating, brush coating, or dip/spin coating, and allowing the solvent to evaporate to leave a film of drug on the

stent surface. In studies performed in support of the invention, a 42-O-alkoxyalkyl rapamycin derivative, 42-O-(2-ethoxyethyl) rapamycin, was applied directly to the surface of a metal stent from an ethyl acetate solution. The drug solution was painted on the stent surface and the solvent was removed by evaporation to leave a film of 42-O-(2-ethoxyethyl) rapamycin on the stent. The drug film was sufficiently adherent to permit catheter implantation of the stents into pigs and retention of the drug on the stent surface for release. A membrane can be optionally applied over the drug film to change the drug release characteristic. Polymer membranes can be formed by dip coating or spray coating, as is well known in the art. The membrane can also be applied to the stent surface by a vapor deposition process or a plasma polymerization process. In one exemplary embodiment, a ~~polytetraflyoroethylene~~polytetrafluoroethylene (Teflon®) or parylene film is formed by vapor deposition as is well known in the art, to modify the drug release rate from the stent. Other suitable polymers and nonpolymers for formation of diffusion controlling membranes include polyimides (via vapor deposition or by solvent coating), fluorinated polymers, silicones (vapor/plasma or deposition), polyketones (PEEK, etc.), polyether imides, vapor/plasma deposited polyacrylates, plasma polymerized polyethyleneoxide (PEO), and amorphous carbon.

On page 28, please replace paragraph [0107] with the following:

[0107] In another study, stents carrying 42-O-(2-ethoxyethyl) rapamycin in the form of a polymer (poly-dl-lactic acid) coating were prepared for insertion into pigs with a vessel overstretch injury to the coronary artery. Comparative and control stents includes bare metal stents, stents having a polymer coating of poly-dl-lactic acid absent drug, stents carrying rapamycin in a poly-dl-lactic acid polymer coating, and stents carrying everolimus in a poly-dl-lactic acid polymer coating. The stents were inserted into vessels which seriously injured (averaging approximately 36% overstretch injury of the vessel) using an angioplasty balloon. The controlled overstretching using the balloon ~~cathether~~catheter caused severe tearing and stretching of the vessel's intimal and medial layers, resulting in exuberant restenosis

at 28 days post implant. In this way, it was possible to assess the relative effectiveness of the various test compounds presented to the vessels on the same metal stent/polymer platform. At the time of insertion, the extent of overstretch was recorded as a percent balloon/artery (B/A) ratio.

On page 30, please replace Table 1 with the following:

Test Group	Stent length (mm)	Drug load (µg)	Polymer coat (µg)	B/A ratio (%)	Mean lumen loss (mm)	Neointimal area (mm^2)	Average Injury score[1]	Diameter stenosis[2] %
bare stent								
28 days	18.7	-	-	1.33	1.69	5.89	1.9	72.0
6 months	18.7	-	-	1.19	0.40	2.68	1.26	32.7
polymer-coated stent	18.7	-	1300	1.36	2.10	5.82	2.11	70.0
rapamycin – high dose	18.7	325	1300	1.39	1.07	3.75	2.10	55.0
rapamycin – low dose	18.7	180	1300	1.42	0.99	2.80	1.90	43.0
everolimus – high dose								
28 days	18.7	325	1300	1.37	0.84	3.54	1.89	38.0
6 months	18.7	325	1300	1.31	1.15	4.18	2.67	68.5
~~everoliums~~everolimus – low dose	18.7	180	1300	1.36	1.54	3.41	2.10	53.0
everolimus – med. dose	18.7	275	640-780[3]	1.36	0.85	2.97	2.13	45.0
42-O-(ethoxyethyl) rapamycin	15	225	225	1.19	0.62	1.30	1.29	14.8

[1]injury scores quantify the degree of vascular injury based on the amount, length, and depth of tear and is scored using the scale of 1, 2, 3, given above.
[2]a lower score indicates higher efficacy
[3]26% drug to polymer ratio

On page 34, please replace paragraph [0123] with the following:

[0123] For stent placement, each animal was immobilized with an intramuscular injection of 0.5 mg/kg acepromazine, 20 mg/kg ketamine, and 0.05 mg/kg atropine. An intravenous ~~cathether~~catheter was placed in an ear vein, and anesthesia was induced with 5-8 mg/kg thiopental. The animal was intubated and ventilated; anesthesia was maintained with inhaled 1-2% isoflurane. A loading dose of intravenous bretylium tosylate (10 mg/kg) was administered for anti-arrhythmic therapy.